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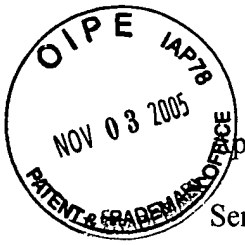


IN THE BOARD OF PATENT APPEALS AND INTERFERENCES

Applicant: Douglas C. Shepard

Serial No.: 10/057,596

Filed: January 24, 2002

Title: MEDICAL ARTICLES HAVING ENZYMATIC SURFACES FOR LOCALIZED THERAPY

Art Unit: 1615

Examiner: Gollamudi Kishore, Ph.D.

Confirmation No.: 2926

Docket No.: 01-531

MAIL STOP APPEAL BRIEF – PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF UNDER 37 C.F.R. §1.192

Sir:

As set forth in the Notice of Appeal filed August 10, 2005 and received by the U.S. Patent Office on August 15, 2005, Appellant hereby appeals the final decision of the Examiner of April 15, 2005 in the above-identified application rejecting the subject matter of the pending claims. Appellant respectfully requests that the Board of Patent Appeals and Interferences reverse the Examiner's rejection of the claimed subject matter. Applicants filed a Pre-Appeal Brief Request on August 10, 2005 and received A Notice of Panel Decision from Pre-Appeal Brief Review on September 29, 2005, resetting the time for filing an Appeal Brief to Saturday, October 29, 2005. Thus, an Appeal Brief is due Monday, October 31, 2005 and is being timely filed.

I. BRIEF ON APPEAL

This appeal is from the examiner's final rejection of April 15, 2005.

II. REAL PARTY IN INTEREST

Scimed Life Systems, Inc. is the assignee of the present invention and the real party in interest.

III. RELATED APPEALS AND INTERFERENCES

No other appeals or interferences within the meaning of 37 C.F.R. § 1.912(c) are known to Appellant, Appellant's legal representative, or the assignees, which will directly affect, be directly affected by, or have a bearing on the Board's decision in the pending appeal.

IV. STATUS OF CLAIMS

This application was filed with Claims 1-32.

Claims 2-10, 25, 26 and 28-32 were withdrawn from consideration pursuant to a requirement for restriction and election of species. Therefore, Claims 1, 11-24 and 27 are currently pending and stand finally rejected.

Claims 1, 13-16 and 19-24 stand finally rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent No. 4,855,234 (Hendrickson), U.S. Patent No. 5,788,678 (Van Antwerp) or Forster et al., Abstract, Am. J. Surg., 156(2):130-2 (August 1988)(Forster), by themselves or in combination, further in view of U.S. Patent No. 5,741,331 (Pinchuk).

Claims 17 and 18 stand finally rejected under 35 U.S.C. §103(a) as being unpatentable over Hendrickson, Van Antwerp or Forster alone or taken together with Pinchuk and further in view of the acknowledged state of the art.

Claims 1, 11-16, 19-24 and 27 stand finally rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,569,688 (Sivan) taken together with Pinchuk.

Claims 17 and 18 stand finally rejected under 35 U.S.C. §103(a) as being unpatentable over Sivan and Pinchuk taken together with the acknowledged state of the art.

Claim 1 is the only independent claim currently rejected. The rejection of Claims 1, 11-24 and 27 is appealed. The pending claims are set forth in Appendix A of this Brief.

V. STATUS OF AMENDMENTS

A Final Office Action was mailed on April 15, 2005, rejecting Claims 1, 11-24 and 27. A Response was filed subsequent to the final rejection on June 15, 2005, and in an Advisory Action mailed on July 5, 2005, the Examiner indicated that the June 15, 2005 Response did not place the application in condition for allowance. The claims have not been amended subsequent to the final rejection.

VI. SUMMARY OF INVENTION

The present invention is directed to compositions and methods for localized delivery of therapeutic agents to the body. Of particular concern are enzymatically active medical articles for localized supply of various therapeutics agents to and localized removal of undesirable chemical entities from a site of interest.

Specifically, independent Claim 1 is directed to the following, with various limitations emphasized:

> 1. An enzymatically active medical article comprising:
> medical article having a matrix disposed on said article, wherein the matrix comprises a block copolymer comprising a polyolefinic block comprising polybutylene and a thermoplastic block comprising a polymers of acrylates, methacrylates or vinyl aromatics, an enzyme disposed within said matrix and at or near a surface of said medical article, such that said medical article is provided with an enzymatically active surface, wherein said matrix allows diffusion of substrates into and diffusion of products out of the matrix, wherein said enzyme is elected from the group consisting of protease enzymes, glycosidase enzymes, enzymes that degrade oxalate, and enzymes that generate NO from arginine.

Advantages of the claimed invention relative to the prior art are as follows (*see* specification on page 3):

Therapeutic agents can be locally supplied to, and undesirable chemical entities can be removed from, a site of interest.

Therapeutic agents can be provided at a site of interest without a significant increase in concentration of therapeutic agent at sites remote from the delivery site.

The medical article provided is self-cleaning.

A marginally or non-therapeutically effective substrate molecule can be converted to a highly therapeutically effective molecule at a local site.

Harmful or potentially harmful substrates can be converted to less harmful species at a local site.

VII. ISSUE

Whether the invention of the appealed claims are patentable in light of the rejections under 35 U.S.C. §103(a) as being unpatentable over one or more of Hendrickson, Van Antwerp, Forster, or Sivan, in view of Pinchuk and acknowledged state of the art.

VIII. GROUPING OF CLAIMS

For purposes of this appeal, the Appellant respectfully submits that the pending claims be considered in one group that may stand or fall together.

IX. ARGUMENT

A. Rejection under 35 USC 103(a)— Henderson, Antwerp, or Forster in view of Pinchuk

Claims 1, 13-16 and 19-24 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Henderson, Antwerp or Forster, each taken alone or in view of Pinchuk US 5,741,331.

The rejection over Hendrickson, Van Antwerp or Forster alone is clearly erroneous because none of these references discloses an enzyme (on an article) disposed within a polymer matrix, as required by the claims, or the specific block copolymers claimed. Further, there is no suggestion in these references to modify the enzymes and coatings of these references to result in the pending claims, either singly or in combination or that there is any reasonable expectation of success that combining the teachings will result in the claimed polymer articles.

Appellant also asserts that the Examiner has failed to establish a *prima facie* case of obviousness. For a reference or combination of references to support a *prima facie*

case of obviousness, three basic criteria must be met: (1) there must be some suggestion and/or motivation to make the necessary modification of the teaching of the reference or references combined to result in the pending claims; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claim limitations. MPEP § 2142-2143; *see In re Jones*, 958 F.2d 347, 351, 21 U.S.P.Q.2d 1941, 1943-44 (Fed. Cir. 1992); *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q. 1596, 1598-99 (Fed. Cir. 1988).

It is respectfully submitted that the rejection based only on these references is improper on its face. The Examiner has presented no reasoning to support a conclusion of obviousness for a medical device (stent or any prosthetic article) coated with the recited polymer matrix within which an enzyme of any type is disposed, much less enzymes of the type claimed in the instant invention. *See* MPEP § 706.02(j)(D) and the cases cited therein.

The Examiner has failed to recognize the structural significance of Appellant's claimed polymeric matrix article wherein an enzyme is an integral part of the polymeric matrix and not merely coated or immobilized onto a solid substrate. The Examiner fails to appreciate the purpose articulated in claim 1 which the cited references do not teach or even suggest: that is, creating enzyme activity in the matrix while at the same time, allowing diffusion of substrates into and diffusion of products out of the matrix. This is achieved by providing a structure having the claimed "enzyme disposed within said matrix." Appellant has discovered that when the enzyme is disposed within a polymer matrix at or near a surface of said medical article, the enzyme is held "in place, while at the same time allowing diffusion of substrates into and diffusion of products out of the matrix." (specification, paragraph [0030]).

In addition, the structure of the polymers recited in the appealed claims is not a random design choice. The recited co-block polymers have been carefully chosen by Appellant to provide the claimed function of "diffusion of enzymatic substrates into, and diffusion of enzymatic products out of the matrix."

Since none of the three primary references of record discloses an enzyme disposed within a polymer matrix, or the particular polymer materials, as required by the instant claims, the Examiner has taken the position that "immobilized" enzymes or

"encapsulating coatings" of the cited art are obvious modifications of the claimed enzyme matrix. However, the Examiner has presented no reasoning to show how "immobilization of enzymes" or "encapsulating coatings" of the cited references renders the claimed polymer matrix with enzymes disposed within the matrix obvious. *See* MPEP § 706.02(j)(D) and the cases cited therein.

Hendrickson discloses enzymes "immobilized on the surface" of a fibrous support that is then "coated" with a polymer (*see* Hendrickson, col. 3, line 53 to col. 4, line 29). The articles formed are used in a method for disinfecting contact lenses. Specifically, they neutralize excess hydrogen peroxide in the disinfecting solution. Polymers suitable for use as the fibrous supports are disclosed at column 5, lines 46-63. No block copolymers of any type are disclosed.

Appellant asserts that coating such an immobilized enzyme with a polymer, as taught by Hendrickson, would result in an enzyme being disposed under a matrix, rather than within a matrix as claimed and would fail to have the claimed structure and/or function.

Similarly, Van Antwerp discloses an enzyme bound to the surface of a catheter that is then coated with a polysilicone or starch based "encapsulating coating" (*see* Antwerp, col. 5, lines 4-8). There is no disclosure of incorporation of the enzyme within a matrix or any block copolymers of any type.

Forster merely discloses an enzyme coated (immobilized) directly on a vascular prosthesis itself. A surfactant is used to immobilize the enzyme. There is no disclosure of incorporating the enzyme in a polymer matrix of any type. Further, there is no teaching of a polymeric matrix below, around or above the enzyme.

The Examiner further turns to Pinchuk for its purported teaching of relevant polymers for various types of implantable articles. *See* column 1, lines 33-40. Pinchuk discloses block and star copolymers for various types of implantable medical devices. However, Pinchuk fails to remedy the deficiencies in Henderson, Antwerp and Forster that are cited above. There appears to be no teaching in Pinchuk of an enzymatically active polymeric matrix, nor does there appear to be any teaching regarding diffusion of enzymatic substrates into, and diffusion of enzymatic products out of, a matrix. Thus, the Henderson, Antwerp and Foster references, either singly or in combination with

Pinchuk, fail to establish a *prima facie* case of obviousness. Accordingly, reconsideration and withdrawal of the rejections of claims 1, 13-16 and 19-24 as being unpatentable over Hendrickson, Antwerp or Forster, each taken alone or in view of Pinchuk, are therefore requested.

Based on the cited references, the Examiner has also failed to explain why there would have been a reasonable expectation of success of producing the claimed medical articles from these teachings. *See* MPEP 2143.02 and the cases cited therein. The Examiner also failed to show how the cited references teach or suggest the claimed functional limitations regarding the "diffusion" action of the enzymatic substrates.

Thus, there can be found within the combination of references no suggestion or motivation to use the polymers of Pinchuk in the devices of the other references. *In re Jones*, *supra*, *In re Fine*, *supra*. Thus, to make such a combination and make a conclusion of obviousness could only be based on the use of undue hindsight, which has long been held to be impermissible. See, for example, *Akso N.V. v. U.S. International Trade Commission*, 808 F.2d 1241, 1480-81, 1 U.S.P.Q.2d, 1241, 1246 (Fed. Cir. 1986), *cert. denied,* 482 U.S. 909 (1987); *Loctite Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 874, 228 U.S.P.Q. 90-99 (Fed. Cir. 1985).

For at least these reasons, it is respectfully submitted that claim 1 is patentable over the cited references. Claims 11-24 and 27 depend upon claim 1 and are therefore patentable for at least the same reasons as is claim 1.

B. Rejection under 35 U.S.C 103(a)---Hendrickson, Van Antwerp or Forster in view of Pinchuk and Acknowledged State of the Art

Claims 17 and 18 have been rejected under 35 U.S.C 103(a) as being unpatentable over Hendrickson, Van Antwerp or Forster by themselves or in combination further in view of Pinchuk and the acknowledged state of the art.

Appellant states that the limitations added by claims 17 and 18 rely on techniques that were generally known. However, these rejections fail at their crux for the reasons discussed above with respect to the other rejections.

Claims 17 and 18 depend upon claim 1 and are therefore patentable for at least the same reasons as is claim 1.

C. Rejection under 35 USC 103(a)—Sivan in view of Pinchuk

Claims 1, 11-16, 19-24 and 27 have been rejected under 35 U.S.C. 103(e) as being unpatentable over Sivan in view of Pinchuk.

Appellant asserts that this rejection is also clearly erroneous because Sivan does not disclose either the claimed copolymers and does not teach the claimed enzyme disposed within a polymeric matrix. Sivan does disclose a medical device bearing an enzyme. However, the enzyme is either bonded directly to the surface of the article or is entrapped within a hydrogel. The only hydrogel disclosed is an interpolymer of an acryloxysilane, diacrolyl polyethylene glycol and the enzyme itself (col. 5, lines 4-9), that together form a polymeric hydrogel network. Thus, in Sivan, the enzyme is the matrix, rather than disposed within a matrix, as claimed. Since the "enzyme" is one of the monomers from which the hydrogel is formed, it is not disposed within a specifically recited polymer matrix, as in the rejected claims. Furthermore, the monomers with which the enzyme is copolymerized in Sivan would not meet the terms of the copolymer blends recited in the rejected claims and are not even remotely similar. Thus, combination of this reference with Pinchuk could not establish a *prima facie* case of obviousness in light of the above cited prior decisions.

The other polymers disclosed at column 3 and referred to by the Examiner constitute the materials from which the body of the stent itself is made. They are not used as a polymeric matrix to carry the enzyme.

Regarding Pinchuk, Pinchuk does not teach or suggest the property of diffusion of substances in and out of a polymer matrix recited in the appealed claims. Thus, the combination of that disclosure with the disclosure of Sivan would at best result in a stent made of those polymers, and not the subject matter of the instant claims. Even if it were possible to combine the references to result in the claimed invention, which it does not appear to be, such combination would be guided by no suggestion or motivation found in the references and would rely on undue hindsight as discussed above.

D. Rejection under 35 USC 103(a)—Sivan in view of Pinchuk and acknowledged state of the art

Claims 17 and 18 have been rejected under 35 U.S.C 103(a) as being unpatentable over Sivan in view of Pinchuk and the acknowledged state of the art.

As discussed previously, Appellant's acknowledgement as to the state of the art with respect to the added limitations of these claims does not remedy the fundamental errors in the basic rejection over the references.

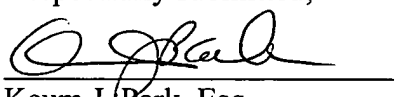
X. CONCLUSION

The references relied on by the examiner do not support a *prima facie* case of obviousness. Thus, it is respectfully submitted that reversal of the rejections of record is in order.

XI. FEES

Appellant's undersigned representative hereby authorizes the required fee for an Appeal Brief, set forth in 37 CFR §1.17(c) to be charged to deposit account No. 50-1047. In addition, any deficiencies may be charged to deposit account No. 50-1047.

Respectfully submitted,



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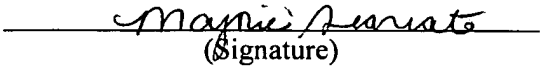
Marjorie Scariati
(Printed Name of Person Mailing Correspondence)



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Appendix A

1. (Previously presented) An enzymatically active medical article comprising:
a medical article having a matrix disposed on said article, wherein the matrix comprises a block copolymer comprising a polyolefinic block comprising polybutylene and a thermoplastic block comprising polymers of acrylates, methacrylates or vinyl aromatics, an enzyme disposed within said matrix and at or near a surface of said medical article, such that said medical article is provided with an enzymatically active surface, wherein said matrix allows diffusion of substrates into and diffusion of products out of the matrix, wherein said enzyme is elected from the group consisting of protease enzymes, glycosidase enzymes, enzymes that degrade oxalate, and enzymes that generate NO from arginine.

2. (Withdrawn) The enzymatically active medical article of claim 1, wherein said enzyme is a protease enzyme.

3. (Withdrawn) The enzymatically active medical article of claim 1, wherein said enzyme is an enzyme that degrades cholesterol esters.

4. (Withdrawn) The enzymatically active medical article of claim 3, wherein said enzyme is selected from cholesterol esterase and cholesterol oxidase.

5. (Withdrawn) The enzymatically active medical article of claim 1, wherein said enzyme is an enzyme that converts hydrocortisone to cortisone.

6. (Withdrawn) The enzymatically active medical article of claim 5, wherein said enzyme is a hydrocortisone esterase enzyme.

7. (Withdrawn) The enzymatically active medical article of claim 1, wherein said enzyme is a glycosidase enzyme.

8. (Withdrawn) The enzymatically active medical article of claim 7, wherein said enzyme is an α-galactosidase enzyme.

9. (Withdrawn) The enzymatically active medical article of claim 7, wherein said enzyme is a β-galactosidase enzyme.

10. (Withdrawn) The enzymatically active medical article of claim 7, wherein said enzyme is a β-glucosidase enzyme

11. (Original) The enzymatically active medical article of claim 1, wherein said enzyme is an enzyme that generates NO from arginine.

12. (Original) The enzymatically active medical article of claim 11, wherein said enzyme is nitric oxide synthetase.

13. (Original) The enzymatically active medical article of claim 11, wherein said enzyme is provided within a biocompatible, biostable matrix coating disposed on said medical article.

14. (Original) The enzymatically active medical article of claim 11, wherein said enzyme is attached to a surface of said medical article.

15. (Original) The enzymatically active medical article of claim 14, wherein said enzyme is covalently attached to a surface of said medical article.

16. (Original) The enzymatically active medical article of claim 14, wherein said enzyme is attached to a surface of said medical article by ion exchange forces.

17. (Original) The enzymatically active medical article of claim 14, wherein said enzyme is attached to a surface of said medical article by antibody-antigen interactions.

18. (Original) The enzymatically active medical article of claim 14, wherein said enzyme is attached to a surface of said medical article by nucleic-acid hybridization.

19. (Original) The enzymatically active medical article of claim 14, wherein said enzyme is attached to a surface coating on said medical device.

20. (Original) The enzymatically active medical article of claim 1, further comprising an enzyme-free coating layer provided over said enzyme, wherein said enzyme-free coating layer acts to hide said enzyme from immune surveillance.

21. (Original) The enzymatically active medical article of claim 1, wherein said medical article is a vascular medical device.

22. (Original) The enzymatically active medical article of claim 1, wherein said medical article is selected from a catheter, a guide wire, a balloon, a filter, a stent, a stent graft, a cerebral aneurysm filler, a vascular graft, a heart valve, a bandage and a bulking agent.

23. (Original) A therapeutic method comprising:

providing the enzymatically active medical article of claim 1; and

administering said medical article to a patient.

24. (Original) The therapeutic method of claim 23, wherein said medical article is a vascular medical device.

25. (Withdrawn) The therapeutic method of claim 23, wherein said enzyme is an enzyme that converts hydrocortisone to cortisone and wherein said medical article is administered to a site of inflammation.

26. (Withdrawn) The therapeutic method of claim 23, wherein said enzyme is an enzyme that converts hydrocortisone to cortisone and wherein said medical article is administered to a site of inflammation.

27. (Original) The therapeutic method of claim 23, wherein said enzyme is an enzyme that generates NO from arginine and wherein said medical article is administered to a site within the vasculature to prevent restenosis.

28. (Withdrawn) The therapeutic method of claim 23, wherein said enzyme is an enzyme that acts upon cholesterol esters and wherein said medical article is placed adjacent atherosclerotic plaque within the vasculature to degrade the cholesterol ester deposits found in said atherosclerotic plaque.

29. (Withdrawn) The therapeutic method of claim 23, wherein said enzyme is a glycosidase enzyme effective to degrade ceramide trihexoside in the treatment of Fabray's disease and wherein said medical article is a blood contacting device.

30. (Withdrawn) The therapeutic method of claim 23, wherein said enzyme is a glycosidase enzyme effective to degrade glycocerebroside in the treatment of Gaucher's disease and wherein said medical article is a blood contacting device.

31. (Withdrawn) The therapeutic method of claim 23, wherein said enzyme is a glycosidase enzyme effective to degrade ganglioside GM2 in the treatment of Tay-Sach's disease and wherein said medical article is implanted within the cranium.

32. (Withdrawn) The therapeutic method of claim 23, wherein said enzyme is oxalte oxidase and wherein said medical article is a urinary catheter.